J. Am. Chem. Soc. 1991, 113, 2533-2537

Supramolecular Transport of Metal Ammine and Amine Complexes through Chloroform Membranes by the Natural Ionophore Lasalocid A. The Selective Enantiomeric Transport of Chiral Metal Complexes

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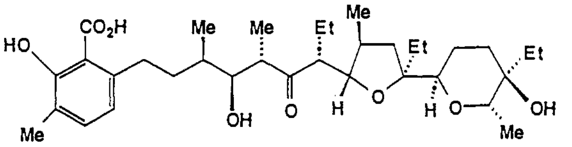
Abstract: The naturally occurring polyether antibiotic lasalocid A acts as a carrier for the transport of inert ammine and amine complexes of Co(III) and Pt(IV) from an aqueous source phase to an aqueous receiving phase across a chloroform membrane. For such systems, "uphill" transport occurs in the presence of a counter gradient of ammonium ions. Thus, under the conditions employed, the transport of the hexaamminecobalt(III) ion across the chloroform membrane phase proceeds to completion over 148 h. Comparative extraction experiments from an aqueous source phase (in the presence and absence of ammonium chloride) into a chloroform phase confirmed that the ammonium ion acts as an effective competitive binder for the lasalocid anion. Lasalocid has also been shown to act as an ionophore for the selective enantiomeric transport of the $[Co(1,2\text{-diaminoethane})_3]^{3+}$, μ-*cis*-$[Co(\text{diethylenetriamine})_2]^{3+}$, and $[Co(1,3,6,8,10,13,16,19\text{-octaazabicyclo}[6.6.6]\text{eicosane})]^{3+}$ cations. In each case partial resolution of the racemic mixture, originally in the source phase, was achieved after the respective transport experiments had proceeded for 6 h. Under the conditions employed, the enantiomeric excess in the receiving phase was 10% for the complex of 1,2-diaminoethane, 27% for that of diethylenetriamine, and 16% for the complex of 1,3,6,8,10,13,16,19-octaazabicyclo-[6.6.6]eicosane. These results demonstrate the potential of the transport technique for achieving chiral discrimination between the optical isomers of suitable metal complexes. Overall, the study represents a novel extension within the area of host–guest chemistry as well as pointing the way for the more general use of transport behavior for the separation and/or sensing of metal complexes.

The use of synthetic and naturally occurring ionophores to transport metal ions[2,3] and, to a lesser extent, organic cations[4] across hydrophobic liquid membranes has been the subject of a large number of investigations. For example, the naturally occurring carboxylic ionophore lasalocid A (**1**) has been demonstrated to facilitate the transport of such cations.[5-7]



(1)

Crystalline lasalocid A complexes of a number of metal ions and organic amine cations have been isolated.[8-12] In such species, one or more molecules of the anionic form of lasalocid bind to the cation such that the resulting host–guest complex has a hydrophobic exterior. The X-ray structure of one such lasalocid anion/amine cation complex shows that the amine cation binds to the lasalocid anion via three $N-H\cdots O$ hydrogen bonds;[10] the lasalocid maintains its (usual) cyclic conformation.

Outer sphere (supramolecular) complexes of the lasalocid A anion and a number of metal ammine and amine complexes have been isolated;[9,13] these include $[Co(NH_3)_6](LAS)_3$, $[Co(NH_3)_5Cl](LAS)_2$, $[Cr(NH_3)_6](LAS)_3$, $[Pt(NH_3)_6](LAS)_4$, and $[Co(en)_3](LAS)_3$ (where LAS is the lasalocid anion and en is 1,2-diaminoethane). The X-ray structure of $[Co(NH_3)_6](LAS)_3$ shows that three lasalocid anions (in cyclic conformations) surround the cobalt complex such that the overall shape is approximately spherical.[13] As a consequence of its hydrophobic outer surface, the adduct is soluble in nonpolar solvents such as chloroform. The $LAS/[Co(NH_3)_6]^{3+}$ interactions involve a network of hydrogen bonds. Similar hydrogen bonding networks have been found in the host–guest complexes formed between particular metal ammines and crown ethers.[14] Indeed, crown ether ionophores incorporating proton-ionizable groups have been shown recently to facilitate the hydrophobic membrane transport of Co(II) and Ni(II) from a source phase consisting of ammonium hydroxide (pH 12).[15] The evidence indicates that transport to

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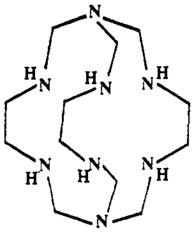
the acid receiving phase involves adduct formation between the crown ionophore and the respective metal(II) ammine species.

Chiral recognition of optically active organic substrates by a range of synthetic and natural ionophores has been well-documented.[16,17] Similarly, synthetic chiral macrocycles have been used as ionophores for the selective enantiomeric transport of a number of optically active guests such as asymmetric ammonium ions.[18] In previous studies, it has been shown that lasalocid[19] forms stable adducts with both optical isomers of a number of metal ammine complexes;[9] lasalocid has also been employed for the optical resolution of chiral amines by fractional crystallization of their lasalocid salts.[10]

We now report examples of the transport (including chiroselective transport)[18] of discrete metal ammine and amine complexes across chloroform membranes using lasalocid A as the ionophore. The documented host-guest complex formation[9,13] between this antibiotic and the series of inert cationic metal complexes mentioned earlier provided the motivation for the present study.

Experimental Section

Reagents. Unless otherwise specified, reagents and solvents were of analytical grade. Lasalocid A was obtained as its sodium salt from Aldrich Chemical Co. and was used without further purification. Stock solutions of this antibiotic for use in the transport and extraction experiments were prepared by dissolving weighed amounts in chloroform which had been previously saturated with water. $[Co(NH_3)_6]Cl_3$, $[Co(NH_3)_5Cl]Cl_2$, $[Co(en)_3]Cl_3$, μ-*cis*-$[Co(dien)_2](ClO_4)_3$ (where dien is diethylenetriamine), and $[Pt(NH_3)_6]Cl_4$ were all prepared and purified following literature methods; a characterized sample of racemic [(1,3,6,8,10,13,16,19-octaazabicyclo[6.6.6]eicosane)cobalt(III)] chloride, $[Co(sep)]Cl_3$ (where sep has structure **2**),[20] was a gift from Professor A. M. Sargeson of the Australian National University. Stock solutions of these complexes (and of NH_4Cl) for use in the extraction and transport experiments were prepared from conductivity water followed by equilibration of each solution with chloroform prior to use.



(2)

Isolation of $[Co(sep)](LAS)_3\cdot 1.5CHCl_3$. To a solution of 0.940 g (2 mmol) of racemic $[Co(sep)]Cl_3\cdot H_2O$ in water (10 mL) was added a solution of 0.245 g (0.4 mmol) of NaLAS in CH_2Cl_2 (10 mL). The mixture was stirred vigorously at ambient temperature for 2–3 days during which time the CH_2Cl_2 layer developed a pale orange color. The CH_2Cl_2 layer was removed, dried over 5-Å molecular sieves, and then filtered. Subsequent removal of solvent under reduced pressure left an orange material that could be recrystallized by dissolving it in a minimum amount of $CHCl_3$ followed by dilution with nitromethane and cooling to −15 °C. Elemental microanalysis indicated the presence of $CHCl_3$ in the crystals as is found for other complexes containing lasalocid.[9] Anal. Calcd for $[Co(sep)](LAS)_3\cdot 1.5CHCl_3$: C, 60.48; H, 8.37; N, 4.89. Found: C, 60.3; H, 8.5; N, 4.9.

Table I. Distribution Ratios for Extraction of the Ammine and Amine Complexes from Water or Ammonium Chloride Solution into a Chloroform Phase Containing the Sodium Salt of Lasalocid A[a]

	D_m	
compd	0.1 M NH_4Cl[b]	water[c]
$[Co(NH_3)_6]Cl_3$	0.57	0.80
$[Co(NH_3)_5Cl]Cl_2$	0.73	1.00
$[Pt(NH_3)_6]Cl_4$	0.52	0.61
$[Co(en)_3]Cl_3$[d]	0.23	0.84
$[Co(dien)_2](ClO_4)_3$[d]	0.43	0.82
$[Co(sep)]Cl_3$	0.69	0.80

[a] All extractions were run for 6 h; the lasalocid anion concentration in the chloroform phase was 1.25×10^{-2} M. [b] The initial concentration of complex in the aqueous phase was 5×10^{-3} M. This phase was also 0.1 M in NH_4Cl. [c] The initial concentration of complex in the aqueous phase was 5×10^{-3} M. [d] Initially present as racemic mixtures.

Extraction Experiments. Extraction of the metal complexes from water and from an aqueous NH_4Cl solution (0.1 M) into chloroform containing the sodium salt of lasalocid A was performed in capped glass vials which were shaken gently for 6 h at 25 ± 1 °C (preliminary runs using longer shaking times confirmed that equilibrium was established within 6 h). The shaker consisted of a horizontally oscillating platform on which were placed the vials. All experiments were performed in duplicate or triplicate and the respective results averaged; further details of the conditions employed for individual extractions are given in Table I.

Transport Experiments. The transport cell design was based on that of Fabbrizzi et al.[21] and consisted of a cylindrical glass tube sealed at one end into which a Teflon dividing plate had been inserted such that the two halves are connected by a gap between the closed bottom of the tube and the plate. The chloroform phase occupied the bottom of the cell under the source and receiving (both aqueous) phases which were separated by the Teflon plate. The interfacial area (for each half of the cell) was 4.9 ± 0.5 cm². The volume of each phase was 20 mL, and each phase was stirred independently; the temperature was maintained at 25 ± 0.1 °C. The receiving phase was made 0.1 M in ammonium chloride; under the conditions of the experiments, no transport was observed when the receiving phase consisted solely of conductivity water.

Solution Analysis. The change in complex concentration in the aqueous phases in the transport and extraction experiments was determined spectrophotometrically with a Cary 219 or a Hewlett Packard 8451A UV-vis spectrophotometer. The concentrations of the respective cobalt species were calculated from measured absorbances and extinction coefficients [determined for each complex in NH_4Cl solution (0.1 M) at the peak maxima in the visible region]. For most transport experiments, a spectrum of the receiving phase (referenced to 0.1 M NH_4Cl solution) was recorded after the run was complete in order to confirm that the respective complexes had been transported intact across the membrane. In experiments for which the "rate" of transport was monitored, the concentrations of the complex in the aqueous source and receiving phases were determined at intervals during the transport run. A small volume (~2 mL) of solution was withdrawn from each of the above phases and the absorbances determined before returning the solutions to the appropriate part of the cell. All absorbances were recorded at room temperature. For the runs involving $[Pt(NH_3)_6]Cl_4$, the platinum concentrations in the aqueous phases were determined following the ICP technique.

Optical Rotations. The optical rotations of the aqueous phases containing $[Co(en)_3]Cl_3$, μ-*cis*-$[Co(dien)_2](ClO_4)_3$, and $[Co(sep)]Cl_3$ were determined with Perkin-Elmer Model 141 or P241 polarimeters and a 10-cm cell maintained at 25.0 ± 0.5 °C. The measurements were made at five wave lengths: the Na line at 589 nm and the Hg lines at 578, 546, 436, and 365 nm. Measured rotations were converted to enantiomeric purity (see Table II) using, for $[Co(en)_3]I_3$, the specific rotation measured for the levo isomer in 0.1 M NH_4Cl $\{[\alpha]^{25}_{436} = +1512 \pm 4°\}$. For example, a typical observed rotation at 436 nm for the receiving phase in a 10-cm cell was +0.029 ± 0.002°; the enantiomeric purities derived from measurements at four other wavelengths, although of lower accuracy since smaller rotations were involved, were still within experimental error of the value quoted in Table II. The specific rotation for μ-*cis*-$[Co(dien)_2](ClO_4)_3$ (at 546 nm) was taken from the published[22] optical

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Table II. Results of Lasalocid Mediated Transport of Inert Metal Ammine and Amine Complexes through a $CHCl_3$ Bulk Liquid Membrane after 6 h at 25 °C[a]

complex	initial S.P. concn, 10^{-3} M	av flux rate, 10^{-7} mol h^{-1} cm^{-2}	% enantiomeric purity (receiving phase)	% transport
$[Co(NH_3)_6]Cl_3$	10.0[b]	4.3 ± 0.1		6.3
$[Co(NH_3)_5Cl]Cl_2$	10.0[c]	6.8 ± 0.2		10.0
$[Pt(NH_3)_6]Cl_4$	10.0[d]	3.5 ± 0.2		5.1
$[Co(en)_3]Cl_3$[e]	20.0[f]	5.9 ± 0.8	10 ± 1[g]	4.3
μ-*cis*-$[Co(dien)_2](ClO_4)_3$[e]	20.0[h]	7.1 ± 0.3	27 ± 4[i]	5.2
$[Co(sep)]Cl_3$[e]	20.0[j]	8.4 ± 0.7	16 ± 1[k]	6.2

[a] The lasalocid concentration was 1×10^{-3} M; all values are the mean and average deviation from two to four separate runs; no transport occurred in the absence of lasalocid in the chloroform phase. [b] The initial pH was 6.0 rising to 6.8 at the completion of the run. [c] Initial pH was 4.2. [d] Initial pH 4.9. [e] Racemic mixture. [f] Initial pH 5.9. [g] Corresponds to 55% of Δ isomer, 45% Λ isomer. [h] Initial pH 5.5. [i] Corresponds to 36.5% of Δ isomer, 63.5% of Λ isomer. [j] Initial pH 6.0. [k] Corresponds to 58% of Δ isomer, 42% of Λ isomer.

rotatory dispersion curve for this complex; as before, enantiomeric purity derived from measurements at other wavelengths agreed within experimental error with the value quoted in Table II. In a similar manner, the literature[20] specific rotations for $[Co(sep)]Cl_3$ were used in the determinations of its optical purity.

Results and Discussion

Isolation of $[Co(sep)](LAS)_3$. By using a related procedure to that employed previously[9] to obtain LAS^- adducts of a number of ammine and amine complexes it proved possible to isolate the corresponding adduct of $[Co(sep)]^{3+}$ (as its chloroform solvate). Microanalytical data confirmed the expected 1:3 (complex:LAS^-) nature of the adduct; it appears likely that this stoichiometry is maintained in the respective solution studies involving adduct formation by $[Co(sep)]^{3+}$ described below.

Extraction of Metal Ammine and Amine Complexes. The relative extractabilities of the respective metal complexes from water and aqueous NH_4Cl (0.1 M) into a chloroform/LAS organic phase were determined. The partitioning of the metal complexes between the aqueous and organic phases may be expressed in terms of a distribution ratio, D_m:

$$D_m = [ML_n]_{(org)}/[ML_n]_{(total)}$$

where $[ML_n]$ is the metal ammine or amine complex. In a simple two-phase system, $[ML_n]_{(org)}$ is the difference between the final and initial aqueous complex concentrations.

The extraction data are summarized in Table I; in each case no extraction occurred in the absence of lasalocid. Clearly, the presence of ammonium chloride in the aqueous phase inhibits the extraction of the respective metal complexes—undoubtedly reflecting competitive binding of the ammonium ion with the lasalocid anion. Indeed, the ammonium ion and lasalocid have been shown previously to yield a solid 1:1 adduct.[11] Under similar conditions, the respective values of D_m show only moderate variation from one metal complex system to the next; for the data relating to extraction from water, there is a correlation between the charge on the complex ion and the corresponding D_m value. As might be expected, the most highly charged complex ion, $[Pt(NH_3)_6]^{4+}$, is the most difficult to extract from the water phase presumably because of its charge and high extent of aquation (it also involves interactions with four LAS ions at the water/chloroform interface and such a process is less favored statistically than for the other complexes where 3:1 and 2:1 adducts are presumed to form). In keeping with this observation, the divalent cation is the most readily extracted with the respective trivalent ions each having similar D_m values which fall between those for the divalent and tetravalent complex ions. For the extractions from ammonium chloride, the situation is more complex because competitive equilibria, involving binding of the ammonium cation to LAS, are present. In view of this, it seems inappropriate to speculate further on the reasons for the observed order of extractability in systems of the latter type. However, the results from the extraction experiments have been shown to serve as useful indicators of the likely success or otherwise of related transport experiments (even though no necessary direct correlation between the degree of extraction and the efficiency of transport is expected).[23] Thus, lasalocid acts as an effective ionophore for the transport of each of the metal complexes listed in Table I (see below). In contrast, under similar conditions to those employed in the present study, monensin was ineffective for the extraction as well as the transport of the $[Co(NH_3)_6]^{3+}$ ion: an attempt to isolate a solid adduct was also unsuccessful.

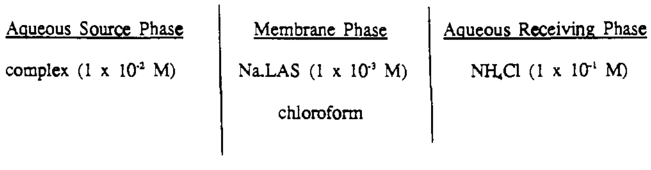

Figure 1. Arrangement of the phases for the transport of the metal ammine complexes.

In the case of $[Co(en)_3]^{3+}$, μ-*cis*-$[Co(dien)_2]^{3+}$, and $[Co(sep)]^{3+}$, which were initially present as racemic mixtures, additional extraction experiments were performed in order to investigate any chiroselective behavior which may occur. Higher initial metal complex and/or lasalocid concentrations were employed for these experiments in order to aid the quantification of such behavior. For the first two systems the extractions were carried out with an initial metal complex concentration of 1×10^{-2} M (5×10^{-3} M in each isomer) and a lasalocid concentration of 2.5×10^{-2} M. For $[Co(sep)]^{3+}$ an overall complex concentration of 5×10^{-3} M was employed with a lasalocid concentration of 2.5×10^{-2} M. Each experiment was run over 6 h, with 0.1 M NH_4Cl present in the aqueous phase.

The results show that one optical isomer is preferentially extracted from the racemic mixture in each case. The selectivity can be expressed in terms of a selectivity factor, K_s, defined as follows:

$$K_s = D_m(\text{most extracted isomer})/D_m(\text{least extracted isomer})$$

For the racemic $[Co(en)_3]^{3+}$ ion, under the conditions employed, there is preferential extraction of the Δ isomer (K_s = 1.13). However, it is the Λ isomer of μ-*cis*-$[Co(dien)_2]^{3+}$ which is preferentially extracted (K_s = 1.42). For $[Co(sep)]^{3+}$, it is the Δ isomer (with K_s = 1.26).

Transport of Metal Ammine and Amine Complexes. In the initial study, successful transport of $[Co(NH_3)_6]^{3+}$ across a chloroform/LAS membrane was achieved with use of the cell configuration shown in Figure 1. The average transport flux over the 6-h period was (4.3 ± 0.1) × 10^{-7} mol h^{-1} cm^{-2} (mean and average deviation of three experiments); this corresponds to transport of approximately 6.3% of the complex initially in the source phase.

It is noted that in the absence of carrier no transport of the complex was observed. Further, no transport was observed when ammonium chloride was absent from the receiving phase or when it was substituted for by sodium ions or a moderate proton concentration (pH 3–4). These results taken together with those from the extraction experiments suggest that hydrogen bonding between

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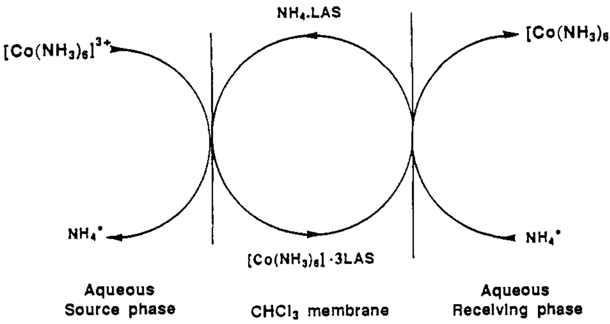

Figure 2. Lasalocid A anion (LAS) mediated transport of $[Co(NH_3)_6]^{3+}$ across a $CHCl_3$ membrane coupled to an NH_4^+ counter gradient.

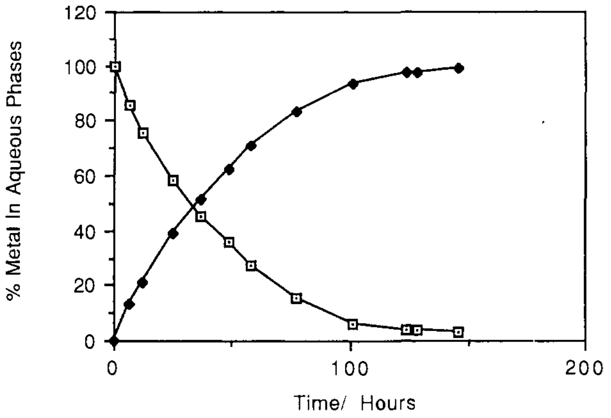

Figure 3. Plot of $[Co(NH_3)_6]^{3+}$ concentration in the aqueous source (□) and receiving (■) phase as a function of time for the lasalocid A mediated transport of this ion at 25 °C.

the ammonium cation and the lasalocid anion plays an important role in "driving" the observed transport. In order to probe this further, a similar concentration of tetramethylammonium chloride was substituted for the ammonium chloride in the receiving phase; no transport was detected in this case. Once again, this result is in agreement with the metal complex transport being driven "uphill" by the reverse ammonium ion transport. The proposed mechanism is shown diagramatically in Figure 2.

As a consequence of the counter flux of ammonium ions across the membrane, it is possible to induce the transport of the Co(III) hexammine complex to proceed to completion. Thus, in a parallel experiment the fall in concentration of the cobalt complex in the source phase and its rise in the receiving phase were determined spectrophotometrically at intervals during the course of the run until the transfer of the cobalt complex from the aqueous source phase to the aqueous receiving phase was essentially complete (Figure 3). The respective aqueous phase concentrations used for this experiment were the same as those employed to determine the average transport fluxes but a higher ionophore concentration (of 2×10^{-3} M) in the membrane phase was employed; this higher concentration resulted in a more rapid approach to equilibrium. At the end of the experiment (after 148 h), the percentage of cobalt complex transported was 98 ± 4% (uncorrected for any complex remaining in the membrane phase).[24] When the above experiment was repeated with a still higher ionophore concentration (of 3×10^{-3} M), the approach to equilibrium was more rapid and occurred in 71 h; it corresponded to transport of 93 ± 5% of the complex originally in the source phase.[25]

A computer fit of the experimental curve for the rise of ammine complex concentration in the receiving phase (see Figure 3) gave

$$Y = 1.77X - 0.01X^2 + (2.15 \times 10^{-5})X^3$$

where Y is the percent complex transported and X is the time in hours. Differentiation of this equation gives an expression for the instantaneous (total) flux across the cell

$$\text{instantaneous flux} = 1.77 - 0.02X + (6.45 \times 10^{-5})X^2$$

The maximum flux rate will occur at zero time when the concentration gradient (across the membrane) is greatest and, from the above expression, this corresponds to a rate of 1.77% of the initial complex concentration per hour (or 3.54×10^{-6} mol h^{-1}). For the cell configuration employed, the rate (J_{max}) per unit area of interface is thus 7.2×10^{-7} mol h^{-1} cm^{-2}. Despite the somewhat different conditions employed, this value is not greatly different from the J_{max} values (of $12.2 \pm 0.6 \times 10^{-7}$ mol h^{-1} cm^{-2}) obtained by Fyles et al.[26] for the transport of a number of potassium salts across a chloroform/cryptand membrane phase. In the latter study, the transport was successfully modelled after assuming that the process is limited by the rate of diffusion of the metal-containing species across the unstirred boundary layers adjacent to the aqueous/organic interfaces. More generally, a similar diffusion mechanism has been assumed to occur in a range of other transport studies;[27] such a mechanism also seems likely to be predominate in the present system.

In view of the above results for $[Co(NH_3)_6]^{3+}$, it was of interest to investigate the transport behavior of related metal ammine cations bearing overall charges other than three. Accordingly, parallel transport experiments were carried out with the cations $[Co(NH_3)_5Cl]^{2+}$ and $[Pt(NH_3)_6]^{4+}$. On the basis of the stoichiometries of the solid adducts,[9] host-guest formation in the membrane phase would be expected to involve two and four lasalocid anions, respectively.[28] Average flux rates across the membrane for these systems are listed in Table II.

Successful preferential transport of the enantiomers of each of the complexes $[Co(en)_3]Cl_3$, μ-*cis*-$[Co(dien)_2](ClO_4)_3$, and $[Co(sep)]Cl_3$ has been achieved. For $[Co(en)_3]Cl_3$, the observed optical rotation of the receiving phase corresponded to 55% of the Δ isomer and 45% of the Λ isomer being present. For the second complex, the resolution was greater with 36.5% of the Δ isomer and 63.5% of the Λ isomer occurring in the source phase. In each of these cases, the optical rotation of the source phase at the end of the experiment (after 6 h) was of similar magnitude but opposite in sign to that measured for the correspondingly receiving phase—thus confirming the internal consistency of the individual experiments. For $[Co(sep)]Cl_3$, partial resolution was again obtained with the observed optical rotation of the receiving phase corresponding to the presence of 57.9% of the Δ isomer and 42.1% of the Λ isomer.

It is noted that the transport selectivities parallel the results from the extraction experiments. The Λ isomer of μ-*cis*-$[Co(dien)_2]^{3+}$ is preferentially extracted into a chloroform phase containing lasalocid and is also selectively transported across the membrane relative to the Δ isomer. In the case of $[Co(en)_3]^{3+}$, the Δ isomer is preferentially extracted and selectively transported relative to the Λ isomer. Again, for $[Co(sep)]^{3+}$, the Δ isomer is preferentially extracted and transported. Although the situation is not rigorously comparable in the present study, the above results are nevertheless in general accord with the model developed by Lehn et al.[29] for the diffusion-limited transport of two substrates, S_A and S_B, in exchange (back) diffusion with a single substrate S_1 (in the present case S_1 would correspond to the NH_4^+ ion). A consequence of the model is that if S_A has a greater extract-

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[24] Further confirmation of the proposed mechanism of transport was obtained by the successful recovery of ammonium chloride from the source phase at the end of the run.

[25] A preliminary investigation of the dependence of the average flux rate (over a 6-h period) on carrier concentration has been carried out. The same conditions were employed as those for the experiments so far described except that a range of ionophore concentrations from 0.05 to 1.0×10^{-2} M were used. The results indicate that the observed increase in average flux with increase in ionophore concentration tends to level out at the higher concentrations of the latter.

[26] Fyles, T. M.; Hansen, S. P. *Can. J. Chem.* **1988**, *66*, 1445.

[27] For recent studies see: Lockhart, J. C. *J. Chem. Soc., Dalton Trans.* **1988**, 1293. Izatt, R. M.; Bruening, R. L.; Bruening, M. L.; Lindh, G. C.; Christensen, J. J. *Anal. Chem.* **1989**, *61*, 1140. Wienk, M. M.; Stolwijk, T. B.; Sudholter, E. J. R.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1990**, *112*, 797.

[28] Preliminary experiments demonstrate that $[Cr(en)_3]^{3+}$ and $[Ni(en)_3]^{3+}$ are transported across a LAS/chloroform membrane confirming that, as expected, the behavior described in this paper applies more widely.

[29] Behr, J.-P.; Kirch, M.; Lehn, J.-M. *J. Am. Chem. Soc.* **1985**, *107*, 241.

ability than S_B ($K_{ex\ A} > K_{ex\ B}$) then the concentration of S_A in the receiving phase will always be greater than that of S_B.

Concluding Remarks. Apart from being a novel development within the area of host guest chemistry, the observation that certain metal complexes can be transported intact across bulk liquid membranes has implications for other areas of chemistry (as well as biochemistry).[30] For example, the technique clearly shows potential for the separation of mixtures of metal complexes and their isomers. In this regard, the present study demonstrates the use of the procedure for the partial resolution of suitable optically active complexes—the latter remains a classical requirement in coordination chemistry which is not always readily met by conventional methods.

Acknowledgment. We thank the Australian Research Council for support and Associate Professor F. R. Keene and Mr. A. J. Leong for assistance. G.W.E. is grateful for the hospitality extended to him at James Cook University during a recent sabbatical leave.

Registry No. 1, 25999-31-9; $[Co(NH_3)_6]^{3+}$, 14695-95-5; $[Co(NH_3)_5Cl]^{2+}$, 14970-14-0; $[Pt(NH_3)_6]^{4+}$, 18536-12-4; $[Co(en)_3]^{3+}$, 14878-41-2; *μ-cis*-$[Co(dien)_2]^{3+}$, 38318-05-7; $[Co(sep)]^{3+}$, 72496-77-6; $[Co(sep)](LAS)_3$, 131656-80-9; $CHCl_3$, 67-66-3; NH_4^+, 14798-03-9.

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(30) Although the respective mechanisms are not yet fully understood, particular microbial iron transport systems have been demonstrated to involve the active transport of intact Fe(III) complexes of natural ligands (siderophores) from outside to inside the cell through the outer cell membrane. For example, this occurs in the case of the Fe(III) complex of enterobactin which forms part of the iron transport system of *Escherichia coli*. See: Raymond, K. N.; Carrano, C. J. *Acc. Chem. Res.* **1979**, *12*, 183. Ecker, D. J.; Matzanke, B. F.; Raymond, K. N. *J. Bacteriol.* **1986**, *167*, 666. Similarly, the active transport of the cobalt complex, vitamin B_{12}, across the outer cell membrane of *Escherichia coli* has also been documented. See: Reynolds, P. R.; Mottur, G. P.; Bradbeer, C. *J. Biol. Chem.* **1980**, *255*, 431.

Calorimetric Determination of the Heats of Protonation of the Metal in (Methyl-substituted cyclopentadienyl)iridium Complexes, Cp′Ir(1,5-COD)

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Received August 13, 1990

Abstract: Titration calorimetry has been used to determine the enthalpies of protonation (ΔH_{HM}) of the iridium in the Cp′Ir(1,5-COD) (Cp′ = $C_5Me_xH_{5-x}$, $x = 0, 1, 3-5$) complexes according to the following reactions: Cp′Ir(1,5-COD) + CF_3SO_3H (0.1 M) → $[Cp'Ir(H)(1,5\text{-}COD)]^+CF_3SO_3^-$, at 25.0 °C in 1,2-dichloroethane. The ΔH_{HM} values become more exothermic from -22.8 ± 0.2 kcal mol^{-1} for Cp′ = C_5H_5 to -28.5 ± 0.2 kcal mol^{-1} for Cp′ = C_5Me_5. A plot of ΔH_{HM} versus the number of Me groups on Cp′ is linear; this result has been interpreted to indicate that the bulkiness of the Me group, even in the C_5Me_5 ligand, probably does not affect the ΔH_{HM} values. Each Me group contributes -1.1 kcal mol^{-1} to ΔH_{HM}. Correlations between ΔH_{HM} and the COD olefin ^1H NMR chemical shift of the Cp′Ir(1,5-COD) compounds and the Ir–H ^1H NMR chemical shift of the protonated species are also made. Equilibrium studies for the protonation of Cp′Ir(1,5-COD) show that the effect of each added Me group on $\Delta G^\ominus$ is -0.89 kcal mol^{-1} and on $\Delta S^\ominus$ is -0.7 eu. Thus, $\Delta S^\ominus$ contributes little to the differences in equilibrium constants for protonation of the Cp′Ir(1,5-COD) complexes. A comparison of the common C_5H_5 and C_5Me_5 ligands shows that the replacement of C_5H_5 by C_5Me_5 increases the equilibrium constant for the protonation of Cp′Ir(1,5-COD) by 1900, makes $\Delta G^\ominus$ more favorable by -4.5 kcal mol^{-1}, causes ΔH_{HM} to be more exothermic by -5.7 kcal mol^{-1}, and reduces $\Delta S^\ominus$ slightly by ca. -4 eu.

Introduction

Currently there is much interest in quantitative measures of the basicities of metals in transition-metal complexes.[1] Yet few data are available for neutral complexes in which the ligands are systematically varied.[1d,f] In this paper, we report the first of a series of such determinations by titration calorimetry in which the basicity is given as the enthalpy of protonation of the transition-metal complex (ΔH_{HM}) with triflic acid (CF_3SO_3H) in 1,2-dichloroethane (DCE) solution at 25.0 °C (eq 1). Previously, we reported enthalpies of protonation (ΔH_{HP}) of several organophosphines using this method.[2]

$$ML_x + CF_3SO_3H \xrightarrow[25.0\ ^\circ C]{DCE} HML_x^+CF_3SO_3^-,\ \Delta H_{HM} \quad (1)$$

Among the types of ligands that are of special interest in organotransition-metal chemistry are the cyclopentadienyl ligand (C_5H_5) and its methyl-substituted analogues ($C_5Me_xH_{5-x}$, $x = 1-5$). Elschenbroich and Salzer[3] summarized some special properties of the pentamethylcyclopentadienyl ligand (C_5Me_5) as compared with C_5H_5. Properties that may affect the basicity of C_5Me_5 complexes relative to their C_5H_5 analogues are "stronger π-donor, weaker π-acceptor properties, increased covalent character of the cyclopentadienyl–metal bond, and kinetic stabilization effected by steric shielding of the metal center." Equilibrium acidities[4] of uncoordinated C_5Me_5H and C_5H_6 in dimethyl sulf-

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